EFFECT OF EXERCISE ON MOLECULAR CORRELATES UNDERLYING LEARNING AND MEMORY

Golding, S, Mohan, RM, Deacon, RMJ*, Girard, I¶, Garland, T¶ and Paterson, DJ, Laboratory of Physiology and *Department of Experimental Psychology, Oxford University, U.K. and ¶Department of Zoology, University of Wisconsin-Madison, U.S.A.

The benefits of exercise on learning and memory processes in the hippocampus are not fully understood. We used DNA microarrays to assess whether exercise affects hippocampal gene expression in a group of mice artificially selected for increased voluntary wheel running. Selected mice (SEL) and also non-selected, randomly bred control animals (CON), all 5-6 weeks old, were assigned into exercise groups (individual cages with wheels, SEL+, n=20 & CON+, n=12) or sedentary groups (individual cages without wheels, SEL-, n=24 & CON-, n=24). Animals were sampled after 0 and 5 weeks of exercise. Hippocampus tissue was stored in RNA*later*™ preservative (Ambion) at –20°C. Atlas™ Mouse 1.2 nylon expression arrays (BD Clontech, UK) were used to assess gene expression. All reagents and protocols for RNA extraction and ^{32}P-labelled array-specific cDNA probe synthesis were supplied and arrays were digitised and analysed using GeneSpring software (Silicon Genetics). Specific genes of interest were further probed using northern blots. Open-field tests were performed to investigate habituation, as a simple measure of non-associative learning and medium-term memory, and locomotor activity.

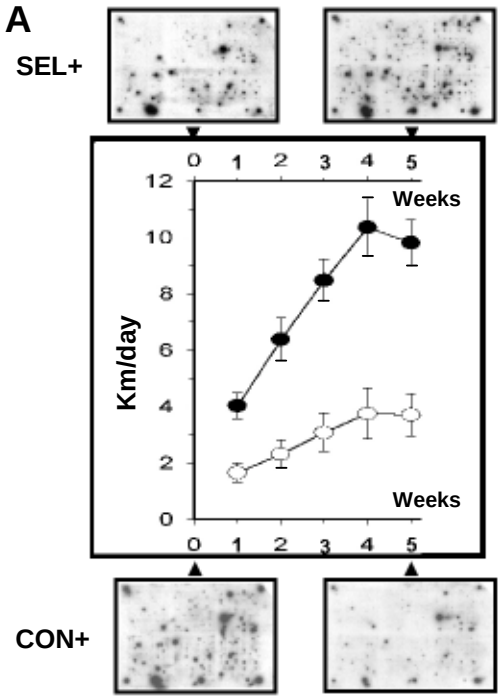

Figure A showing mouse running profiles (• = SEL+, o = CON+, data are means ± SEM) and representative microarray blots for 0 and 5 weeks.

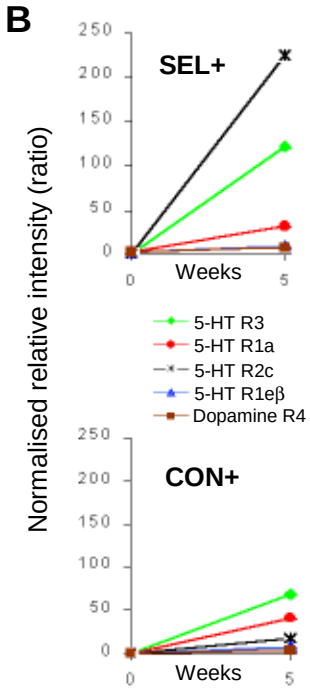

Figure B showing the expression levels of learning- and memory-related genes during this period.

The SEL+ mice ran significantly more when compared to the CON+ group (Figure A). Voluntary exercise by the CON+ group was associated with an improved habituation and memory retention. 543 of the 1176 array genes were expressed in the hippocampus with the running profile of the exercising mice matched by the expression of a cluster of up to 109 of these genes, including several associated with learning and memory (Figure B). The enhanced peak running performance seen with the SEL+ group was, however, associated with impaired memory retention in the open-field test and alterations in patterns of gene expression, including substantial up-regulation in the expression of 5-HT receptors 2c and 3. Previous studies show that removal or inhibition of these genes is correlated with facilitating locomotor and exploratory activity, and with improved memory retention and learning. Our results suggest that the level of physical activity can influence the expression of genes associated with learning and memory.

This work was funded by The British Heart Foundation and the U.S. National Science Foundation. RMJD is funded by The Wellcome Trust.